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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/207,649	12/08/1998	SUSAN LINDQUIST	17481-004001	7099

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EXAMINER

CHERNYSHEV, OLGA N

ART UNIT	PAPER NUMBER
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1649

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11/21/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 09/207,649	Applicant(s) LINDQUIST, SUSAN	
	Examiner Olga N. Chernyshev	Art Unit 1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 01 October 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,3,7-20,22 and 37 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,7-11,14-20,22 and 37 is/are rejected.
- 7) ☒ Claim(s) 3,12 and 13 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|--|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input checked="" type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Response to Amendment

1. Claims 1 and 13 have been amended as requested in the amendment submitted on October 01, 2007. Following the amended, claims 1, 3, 7-20, 22 and 37 are pending in the instant application.

Claims 1, 3, 7-20; 22 and 37 are under examination in the instant office action.

2. Any objection or rejection of record, which is not expressly repeated in this action has been overcome by Applicant's response and withdrawn.

3. Applicant's arguments filed on October 01, 2007 have been fully considered but are not persuasive for the following reasons.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1, 7-11, 14-20, 22 and 37 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for reasons of record in section 6 of Paper mailed on March 29, 2007.

Applicant traverses the rejection on the premise that the instant specification discloses two species of the genus of "mammalian aggregate-prone amyloid protein", which are PrP and β -

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amyloid, and that at the time of invention “the person of ordinary skill in the art [...] was aware that numerous other proteins are [also] able to form amyloid or amyloid-like deposits” (p. 5 of the Response). Applicant refers to a review article in *Nature*, 2004, to recite other amyloid forming proteins (huntingtin, atropine-1, ataxins, androgen receptor, tau, and α -synuclein). Applicant further argues that the rejection is in conflict with the decisions in *Falkner v. Inglis* stating that “[t]he large number of mammalian proteins that were known in the art to form amyloid or amyloid-like deposits are representative of the full scope of the genus encompassed by the term “mammalian aggregate-protein amyloid protein” (p. 6 of the Response). Applicant’s arguments have been given careful consideration but they are unpersuasive for the following reasons.

Claims 1, 7-11, 14-20, 22 and 37 are directed to methods of identifying a candidate substance that inhibits the aggregation of a mammalian aggregate-prone amyloid protein in a yeast cell. The term “aggregate-prone amyloid protein” is defined as “any protein that is able to form an amyloid or amyloid-like deposits” (p. 5 of the specification). The review article of Ross et al., cited by Applicant, defines amyloid as “[t]he [protein] aggregates [which] usually consist of fibers containing misfolded protein with β -sheet conformation” (abstract). The term “amyloid” is defined in the art in association with neurodegenerative diseases, and encompasses specific proteins that are capable of pathological aggregation (aggregate-prone) to form characteristic fibers histologically distinguishable by Congo Red staining, see the last column of Table 1 at p. S11 of Ross et al. article.

However, in the instant case, the claims specifically recite a mammalian aggregate-prone amyloid peptide as a part of a chimeric protein to be expressed in a yeast cell as a necessary

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component to practice the instant claimed method. The Examiner maintains that the claims do not satisfy the written description requirement of 35 U.S.C. 112, first paragraph, because the specification fails to provide sufficient distinguishing identifying characteristics of the genus of "mammalian" proteins. There is no disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. The instant situation is directly analogous with the decision in *University of California v. Eli Lilly and Co.*, where the court held that,

"A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *University of California v. Eli Lilly and Co.*, 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1405 (Fed. Cir. 1997 (bracketed material in original)). The claims in *Lilly* were directed generically to vertebrate or mammalian insulin cDNAs. See *id.* at 1567, 43 USPQ2d at 1405. The court held that a structural description of a rat cDNA was not an adequate description of these broader classes of cDNAs.

The *Lilly* court explained that

a generic statement such as... 'mammalian insulin cDNA,' without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus.

Id. at 1568, 43 USPQ2d at 1406. Finally, the *Lilly* court set out exemplary ways in which a genus of cDNAs could be described:

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A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus.

Id. at 1569.

This standard applies to polypeptides as well as DNAs. *See University of Rochester v. G.D. Searle & Co., Inc.*, 358 F.3d 916, 925, 69 USPQ2d 1886, "893 (Fed. Cir. 2004): "the statute applies to all types of inventions. We see no reason for the rule to be any different when non-genetic materials are at issue."

In the instant case, the claims recite a genus of mammalian aggregate-prone amyloid proteins but the specification provides no description of the members of the genus. There is no structure-function correlation, no identification of distinguishing features that specifically define the genus so that a skilled practitioner would be able to visualize the members of "mammalian aggregate-prone amyloid proteins" from just aggregate-prone amyloid proteins or non-mammalian aggregate-prone amyloid proteins. Applicant submits that two proteins, PrP and β -amyloid, are described as representative species of the genus and that the art discloses at least six more (the Nature article). However, the specification is silent to define as how large the genus of "mammalian aggregate-prone amyloid proteins" is. For example, how many members are within the genus and how representative the recited eight structurally unrelated proteins are of the genus?

Applicant submits that the "aggregate forming domain" (as that term used in claim 7) of a given aggregate-prone amyloid protein is generally known or easily determined by the skilled person by use of routine assays" (p. 6 of the Response). This argument has been fully considered

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but not persuasive because the requirement for written description under the first paragraph of section 112 is separate and distinct from the enablement requirement of that paragraph. See *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1116-17 (Fed. Cir. 1991). Compliance with the written description requirement is a question of fact. *Id.* The specification cannot refer one skilled in the art to an assay to research, discover and identify for themselves what Applicant has invented. If at the time of invention Applicant was in possession of the genus of mammalian amyloid proteins, it should not be a problem to describe in clear terms as how these proteins look like.

Further, with respect to the use of an assay to support written description, in *University of Rochester*, the patent claimed a method of selectively inhibiting the enzyme PGHS-2 (also known as COX-2) by "administering a non-steroidal compound that selectively inhibits activity of the PGHS-2 gene product in a human." *Id.* at 918, 69 USPQ2d at 1888. The patent "described in detail how to make cells that express either COX-1 or COX-2, but not both..., as well as 'assays for screening compounds, including peptides, polynucleotides, and small organic molecules to identify those that inhibit the expression or activity of the PGHS-2 gene product.[']" *Id.* at 927, 69 USPQ2d at 1895.

The court held that the disclosure of screening assays and general classes of compounds was not adequate to describe compounds having the desired activity: without disclosure of *which* peptides, polynucleotides, or small organic molecules have the desired characteristic, the claims failed to meet the description requirement of § 112. *See id.* ("As pointed out by the district court, the '850 patent does not disclose just 'which "peptides, polynucleotides, and small organic

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molecules" have the desired characteristic of selectively inhibiting PGHS-2.'... Without such disclosure, the claimed methods cannot be said to have been described.").

Moreover, just as in the *University of Rochester* case, discussed above, the present application discloses a broad genus of chemical compounds (those aggregate-prone amyloid proteins known to form fibers and be stained by Congo Red) but the claims are limited to only those compounds having a desired characteristic (mammalian aggregate-prone amyloid proteins). Just as in *University of Rochester*, the present specification does not disclose which of many possible amyloid proteins are within the genus of mammalian amyloid proteins and are part of Applicant's invention.

Finally, Applicant's reference to the decision in *Falkner v. Inglis* (p. 6 of the Response) is misplaced. The structure of a "DNA encoding a signal sequence" is, first, within the knowledge of a person of ordinary skill in the art and, second, is not essential to the invention. The instant situation is entirely different. The instant recited "mammalian aggregate-prone amyloid proteins" are essential to produce the critical chimeric proteins and, consequently, to practice the claimed method. For these proteins, the skilled practitioner needs a clear explanation as how the "mammalian aggregate-prone amyloid proteins" look like. On the other hand, similarly to the "signal protein", there is no need to describe the full genus of "detectable marker proteins" (as in claim 7), or "hormone receptor(s)" (claim 10), or "labels" (claim 17), because a skilled artisan knows very well what is encompassed by these limitations, can visualize them and use the species interchangeably as they do not affect the scope of invention.

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The Examiner finds that the disclosure as filed does not provide adequate written description to support the genus of mammalian aggregate-prone amyloid proteins encompassed by the instant claims, and the rejection is maintained.

Allowable Subject Matter

7. Claims 3, 12 and 13 would be allowable if rewritten in independent format.

Conclusion

8. No claim is allowed.
9. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).


A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Olga N. Chernyshev whose telephone number is (571) 272-0870. The examiner can normally be reached on 8:00 AM to 5:00 PM.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey J. Stucker can be reached on (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.


Olga N. Chernyshev, Ph.D.
Primary Examiner
Art Unit 1649

November 19, 2007